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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,177	02/05/2007	Alejandro Balazs	C1233,70001US01	4085
23628 7590 12/07/2009 WOLF GREENFIELD & SACKS, P.C. 600 ATLANTIC AVENUE BOSTON, MA 02210-2206				
EXAMINER				
SGAGIAS, MAGDALENE K				
ART UNIT		PAPER NUMBER		
1632				
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12/07/2009		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/577,177

Applicant(s)

BALAZS ET AL.

Examiner

Magdalene K. Sgagias

Art Unit

1632

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 August 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) 13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-8, 12 is/are rejected.
- 7) ☒ Claim(s) 4, 5 and 9-11 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 April 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-06)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's arguments filed 08/06/2009 have been fully considered. Claims 1-13 are pending. The amendment has been entered. Claim 13 is withdrawn. Claims 1-12 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims **4-5, 9-11** are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only--; and/or, --cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims **1-3, 6-8, 12** are rejected under 35 U.S.C. 102(b) as being anticipated by **Ghannadan et al**, (Int Arch Allergy Immunol, 127: 299-307, 2002).

Ghannadan et al, disclose a) contacting a biological sample of HNC-1 cell line with the mAb for endothelial cell C protein (CD201) and b) separating cells that bind to

the mAb by FACS analysis thereby producing a substantially pure population of EPCR+ hematopoietic stem cells (abstract, p 300 2nd column under flow cytometry; p 302 Table 2 column 1-2, 7 and p 303, 2nd column under phenotype of HNC-1 section) (**claims 1-3, 6-7, 12**).

Thus, Ghannadan et al, anticipate the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of claims 1-12 under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over **Wognum et al**, [Archives of Medical Research 34: 461-475, 2003, (IDS)] is withdrawn since Wognum was published in November-December after the 10/31/03 priority date of the instant invention.

Claims **1-3, 6-8, 12** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Ghannadan et al**, (Int Arch Allergy Immunol, 127: 299-307, 2002) in view of **Goodell et al**, (J Exp Med, 183: 1797-1806, 1996).

Ghannadan et al, disclose a) contacting a biological sample of HNC-1 cell line with the mAb for endothelial cell C protein (CD201) and b) separating cells that bind to the mAb by FACS analysis thereby producing a substantially pure population of EPCR+ hematopoietic

stem cells (abstract, p 300 2nd column under flow cytometry; p 302 Table 2 column 1-2, 7 and p 303, 2nd column under phenotype of HNC-1 section) (**claims 1-3, 6-7, 12**). Ghannadan et al, differs from the present invention for not teaching magnetic bead separation.

However, at the time of the instant invention **Goodell et al** teach the separation of side population (SD) cells which exhibit the highest dye-dye efflux activity and most enriched for hematopoietic reconstitution activity by magnetic bead separation and these cells were shown in competitive repopulation experiments to contain the vast majority of HSC activity from murine bone marrow and to be enriched at least 1,000-fold for in vivo reconstitution activity (abstract and under M&Ms p 1798). Goodell suggests the stem cell purification strategy by the side population strategy can be extended to human adult bone marrow, human umbilical cord blood and porcine bone marrow with Hoechst 33342 and observe a staining pattern remarkably similar to that which observed with routine cells and stained SP cells from human bone marrow with respect to cell surface markers found on human progenitor cells and in vitro culture assays (p 1805).

The combination of prior art cited above in all rejections under 35 U.S.C. 103 satisfies the factual inquiries as set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Once this has been accomplished the holdings in KSR can be applied (*KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. ___, 82 USPQ2d 1385 (2007): "Exemplary rationales that may support a conclusion of obviousness include: (A) Combining prior art elements according to known methods to yield predictable results; (B) Simple substitution of one known element for another to obtain predictable results; (C) Use of known technique to improve similar devices (methods, or products) in the same way; (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results; (E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a

reasonable expectation of success; (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention."

Accordingly, it would have been obvious to the ordinarily skilled artisan to modify the teachings of Ghannadan et al, by utilizing the Hoechst 33342 dye exclusion technology of Goodell in order to obtain a pure enriched population of EPCR+ cells in a biological sample, with a reasonable expectation of success. One of ordinary skill in art would have been motivated to make this modification in order to produce a side population (SD) cells of EPCR+ cells which exhibit the highest dye-dye efflux activity and most enriched for hematopoietic reconstitution activity by magnetic bead separation as taught by Goodell et al.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 1-3, 6-8, 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Ghannadan et al**, (Int Arch Allergy Immunol, 127: 299-307, 2002) in view of **Miyazato et al**, ((Blood, 98:422-427, 2001).

The teachings of Ghannadan et al, apply here as indicted above.

Ghannadan et al, do not teach column chromatography for the production of EPCR+ cells.

However, at the time of the instant invention **Miyazato et al**, teaches that it is routine in the art to isolate hematopoietic cells by column chromatograph. Miyazato et al, teach the PB or

BM aspirates and mononuclear cells (MNCs) were purified from the specimens by the Ficoll-Hypaque density gradient centrifugation, labeled with AC133 MicroBeads and subjected to chromatography on miniMACS magnetic cell separation columns volunteers (p 423 under materials and methods). Portions of the MNC and AC1331 cell preparations were stained with Wright-Giemsa solution, or analyzed with a FACScan flow cytometer for the expression of CD34, CD38, and AC133. The number of blasts purified from the BM of leukemia patients was more than 100 times that purified from the BM of healthy volunteers (p 423 under materials and methods).

The combination of prior art cited above in all rejections under 35 U.S.C. 103 satisfies the factual inquiries as set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Once this has been accomplished the holdings in KSR can be applied (*KSR International Co. v. Teleflex Inc.* (*KSR*), 550 U.S. ___, 82 USPQ2d 1385 (2007): "Exemplary rationales that may support a conclusion of obviousness include: (A) Combining prior art elements according to known methods to yield predictable results; (B) Simple substitution of one known element for another to obtain predictable results; (C) Use of known technique to improve similar devices (methods, or products) in the same way; (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results; (E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention."

Accordingly, it would have been obvious to the ordinarily skilled artisan to modify the teachings of Ghannadan et al, by utilizing column chromatography in order to obtain enriched population of EPCR+ cells in a biological sample, as taught by Miyazato et al, with a reasonable expectation of success. One of ordinary skill in art would have been motivated to make this modification in order to produce a population of EPCR+ cells since Miyazato et suggest the number of blasts purified from the BM of leukemia patients was more than 100 times that purified from the BM of healthy volunteers.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAGDALENE K. SGAGIAS whose telephone number is (571)272-3305. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paras Peter can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from

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a USPTO Customer Service Representative or access to the automated information system,
call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Magdalene K. Sgagias, Ph.D.
Art Unit 1632

/Anne-Marie Falk/
Anne-Marie Falk, Ph.D.
Primary Examiner, Art Unit 1632